Distribution of Heterogenic Reflexes Among the Quadriceps and Triceps Surae Muscles of the Cat Hind Limb

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Wilmink, Ronnie J. H. and T. Richard Nichols. Distribution of heterogenic reflexes among the quadriceps and triceps surae muscles of the cat hind limb. J Neurophysiol 90: 2310–2324, 2003. First published June 25, 2003; 10.1152/jn.00833.2002. Neural signals from proprioceptors in muscles provide length and force-related linkages among muscles of the limbs. The functions of this network of heterogenic reflexes remain unclear. New data are reported here on the distribution and magnitudes of neural feedback among quadriceps and triceps surae muscles in the decerebrate cat. The purpose of this paper was to distinguish whether inhibitory-force feedback is directed against muscles by virtue of the motor-unit composition or articulation of the muscle. These studies were carried out using controlled stretches and measurements of the resulting force responses of individual quadriceps and triceps surae muscles. Responses were evoked over a wide range of background force levels. In agreement with earlier electrophysiological studies, excitatory length feedback strongly linked the vastus muscles, but excitatory reflexes between each vastus and rectus femoris muscles were weak. We also observed a substantial excitatory linkage from the vastus muscles to the soleus muscle. In contrast, force-related inhibition was absent in the heterogenic reflexes among the vastus muscles but strong and bidirectional between each vastus muscle and the rectus femoris muscle and between triceps surae and quadriceps muscles. We conclude that short-latency feedback in the hindlimb is organized according to muscle articulation. Length feedback within muscle groups regulates joint stiffness while interjoint length feedback may compensate for the effects of nonuniform inertial properties of the limb. Force feedback is organized to regulate coupling between joints and, along with length feedback, determine the mechanical properties of the endpoint.

INTRODUCTION

Neural feedback from receptors in skeletal muscle projects back to the muscle of origin as well as to other muscles in both humans and cats (Brooke and McGill 1985; Eccles et al. 1957; Edgley et al. 1986; Koceja 1995; Meunier et al. 1990; Misiaszek and Pearson 1997; Roby-Brami and Bussel 1990). Knowledge of the intermuscular distribution of this feedback is essential to an understanding of the functions of proprioceptive pathways in motor coordination. Recent work (Nichols 1989) based on mechanographic analysis in decerebrate animals (Liddell and Sherrington 1924) has shown the existence of two classes of rapid feedback. Heterogenic length feedback acts with approximately the same time course as the stretch reflex and leads to excitation of muscles with synergistic actions and inhibition of antagonistic muscles (Nichols 1999; Nichols and Koffler-Smulevitz 1991). The magnitudes of these reflexes are essentially independent of background force and, in the triceps surae and pretilial flexor muscles of the cat, correspond to the distribution of group Ia afferents from muscles spindles (Eccles et al. 1957; Scott and Mendell 1976). Because the distribution of group Ia effects appears as a dominant factor in the distribution of this feedback, these pathways are likely to regulate joint stiffness in a directional manner as predicted by an extension of the myotatic unit concept (Nichols et al. 1999).

The other class of heterogenic feedback is inhibitory and increases with active background force in the muscle of origin (Bonasera and Nichols 1994; Nichols et al. 1999). Feedback is widely distributed among antagonist muscles in the hindlimb and appears to arise at least in part from Golgi tendon organs. The principles that govern the distribution of this feedback remain unclear. It has been argued that excitatory force feedback, which is apparently expressed during locomotion (Pearson 1995; Pearson and Collins 1993; Prochazka 1996), is widely distributed among extensor muscles to provide a loading reflex (Dietz and Duysens 2000). Widespread group I excitation has also been observed in the fictive locomotion preparation (Angel et al. 1996; Guertin et al. 1995), although group I excitation may be weak from the quadriceps to the triceps surae muscles. Force-related inhibition, however, is not uniformly distributed across antagonist muscles. Among the triceps surae muscles, inhibitory feedback extends from either gastrocnemius lateralis or medialis (LG or MG) muscles to soleus (SOL) but not between LG and MG (Nichols 1994, 1999). These data suggest that either motor-unit type or articulation govern the distribution of this feedback. Inhibitory-force feedback has also been observed to link the triceps surae muscles with the muscles of ankle stabilization (Nichols 1994), suggesting that the distribution of inhibitory-force feedback links muscles that cross different axes of rotation. Single motor-unit studies have shown that type I motor units in MG are not inhibited by the stretch of MG (Dacko et al. 1996), supporting by exclusion the hypothesis that inhibitory-force feedback links muscles that cross different joints or axes of rotation.

The systems of quadriceps and triceps surae muscles provide a means of further validating our proposed rules governing the distribution of the preceding classes of heterogenic feedback. The quadriceps muscles consist of single joint vastus [vastus...
Each muscle was represented twice per preparation. The vastus muscles contained both homogeneous and heterogeneous fiber types (Ariano et al. 1973). In particular, VI is composed essentially entirely of type I muscle fibers, whereas VM and VL are heterogeneous. Our hypothesis predicts that short-latency force feedback should link RF with each vastus muscle but not link muscles within the vastus group.

In this paper, we describe the relative distributions of excitatory, presumably length feedback and inhibitory-force feedback among the quadriceps and triceps surae muscles. We found the distributions of the two kinds of feedback to be complementary and in line with our predictions. Force feedback linked single-joint with two-joint muscles in the quadriceps group, but these links were bidirectional unlike the unidirectional links in the triceps surae muscles (Nichols 1999). In addition, we provide evidence that the excitatory pathway between the vastus and soleus muscles is substantial and is likely to influence interjoint coordination as well. These results extend our previous results and support our conclusion that short-latency, inhibitory-force feedback links muscles that cross different joints and axes of rotation. In some cases, longer-latency inhibition from VI to VL was also observed, suggesting a network of inhibitory mechanisms that is organized differently from the short-latency inhibition. This work has appeared in a doctoral thesis (Wilmink 1998), and preliminary data supporting these conclusions have been published elsewhere (Nichols 1994; Wilmink et al. 1996, 1997).

**Methods**

The results depicted in this study were drawn from experiments on 12 healthy adult cats of either sex (6 females and 6 males) weighing 3.25–6 kg. In most cases, the studies were conducted on both legs so each muscle was represented twice per preparation.

**Surgery**

Under deep anesthesia using isoflurane gas, an intercollicular decerebration was performed, removing all brain matter rostral to the transection. On both hind legs, the muscles of the quadriceps and triceps surae were separated, and their tendons were connected to individual clamps fixed to strain gauge myographs for the force measurements. Each myograph was mounted by way of a miniature universal joint to a linear slide. The universal joints maintained alignment between each muscle tendon and the moving slide. Muscle lengths were controlled using servo motors that moved the linear slides by way of flexible stainless steel cables clamped to the motor pulleys. The tendency of the cables to unwind and pull back amounted to <1 N and was compensated by unloading the slides with elastic bands. Position feedback was obtained from precision potentiometers mounted in line with the motor shafts. Up to four such actuators were available for these experiments.

The quadriceps muscles, VL, VM, VI, and RF, were separated in each leg in some preparations. During most surgeries, it was possible to separate these muscles with little injury, but in some preparations, it was necessary to sacrifice certain muscles to avoid damaging the adjacent muscle. For instance, VI merged in a complex way with both VL and VM in some cases. Also, the tendon of RF usually merged with VL and VM before inserting on the patella. As a result, VI was included in the study 11 times, RF and VI were included 10 times, and VM 7 times. In some experiments, the quadriceps group (Q) was subdivided into two groups based on articulation, namely, the vastus muscles (V) and RF. Similarly, the triceps surae group was divided into individual muscles, namely, MG, LG, and soleus (S) muscles or in subgroups based on articulation, namely the gastrocnemius muscles (G) and S. In each leg, the posterior tibial nerve was dissected, draped over a hook electrode, and cut distally. Fixation of the leg was accomplished using rods ending in screws, which were inserted into the femur right below the hip and one just above the knee. Hip pins were used to immobilize the pelvis.

The crossed-extension reflex was evoked to recruit all of the muscles of the quadriceps and triceps surae groups. The contralateral posterior tibial nerve was stimulated using 40-Hz monophasic constant current pulses at two times reflex threshold. The initial length of each muscle was set by stretching the muscle until a passive tension of ~1 N was achieved. Data were acquired while the muscles were quiescent as well as when they were activated by the crossed-extension reflex. The stretches were trapezoidal in shape, with a rise- and fall time of 50 ms, amplitude of 2 mm, and a hold phase of 250 ms. Stretch velocity was therefore 40 mm/s. The amplitude of 2 mm was chosen to fall generally in the range of active lengthening during locomotion. The rise time of 50 ms was rapid enough to provide a sufficiently large prereflex force for reliable measurement of the intrinsic mechanical response of the muscle. This measurement was useful to detect the presence of mechanical artifacts.

**Protocols**

Three protocols were used to evaluate autogenic and heterogenic reflexes. In protocol 1, one muscle, the donor, was stretched every 2–3 s during activation using the crossed-extension reflex. Another muscle, the recipient, was held isometrically (Nichols 1999). Any heterogenic reflex effects were detected by increases or decreases in force in the recipient. In protocol 2, stretches of the recipient were performed in alternation with stretches of both donor and recipient as the force decayed (see Fig. 1B). Two groups of records resulted from this protocol, namely, one with stretch of the recipient only and one with stretch of both muscles. Heterogenic reflex effects were detected by changes in the magnitude of the reflexes in the recipient muscle on even-numbered trials. Force responses in the first group were purely autogenic, and responses in the second group consisted of autogenic and heterogenic components. These latter responses were therefore referred to as compound responses. Heterogenic effects present for protocol 2 but not protocol 1 would suggest that these effects are presynaptic. In protocol 3, two muscles were stretched independently and then together (Fig. 1A). In this case, each muscle served as both recipient and donor, resulting in three groups of responses. This protocol was used under quiescent conditions when a large number of trials were possible.
In selected cases, ≤150 μg strychnine was injected intravenously toward the end of the experiment to test whether inhibitory reflexes were likely to be mediated by glycineric pathways (Bonasera and Nichols 1994; Nichols 1999). At the end of each experiment, the animal was killed with an overdose of pentobarbitalsodium (100 mg/kg iv).

A 486-based personal computer sampled the length and force channels (≤8 total) at 500 Hz. The precision of data acquisition was 0.05 N for the force channels and 0.04 mm for the length channels. The same computer provided the servo amplifiers (PMI-Motion Technologies) with the length commands at a constant rate of 2048 Hz/channel through a dedicated 12-bit D/A conversion card.

Quantification of reflex effects

The data were analyzed according to the acquisition protocol (see above) using custom software written in Matlab (Mathworks).

QUIESCENT STATE. The quiescent runs, in which the background force was essentially constant, were acquired using protocol 3 and analyzed by superimposing the averaged autogenic with the averaged heterogenic plus autogenic (compound) force response for that muscle (Fig. 1A). The difference in area under these force traces, in the interval from 10 ms after stretch onset until the end of the hold phase (see Fig. 1A, bottom), was computed and normalized to the area under the autogenic force response. The 10-ms start time for this integration was chosen because reflex effects could not have begun before this time. For each muscle combination ≥10–15 complete runs of data were collected. Figure 1A shows the initial portion of a quiescent run and the resulting averaged responses as an example.

ACTIVATED STATE. The background force in all the activated muscles generally decayed during the crossed-extension reflex to levels observed during the quiescent state, over a time course of 10–60 s. Data were collected for 50 ms prior the onset of stretch using either protocol 1 or 2. The off-line analysis program calculated an estimate of the baseline force for every force response, by computing a linear fit through the first and last 50 ms of data for every trial during data collection. The “force response” is here defined as the difference between the force at the corresponding time points and the estimated baseline force. The force responses were measured every 5 ms during the time course of the trial for the responses at all force levels. Therefore each response measurement was associated with a time point and an initial force as represented in the three-dimensional plots (see following text). For data collected using protocol 1, one group of responses of the recipient muscles resulted. For each of these time points, the relationships of the responses to background force were fitted using quadratic polynomials. The polynomials were plotted together for all time points in the form of three-dimensional surfaces with time and force as independent variables (Fig. 8). Positive values on the vertical axis represent excitatory effects.

For data obtained using protocol 2, two groups of responses were obtained, namely, autogenic and compound (Fig. 1B). Force responses at two particular time points, the end of the ramp (the “dynamic” response, as shown in Fig. 2, A–C) and the end of the hold-phase (the “static” response, as shown in Fig. 2D) were used to represent early and late effects of heterogenic reflexes (Nichols and Koffler-Smulevitz 1991). For each experimental run, these points were graphed against the initial force (force averaged over 5–45 ms prior to stretch) of the donor muscle (Fig. 2) because force-related heterogenic effects are correlated mainly with force of the donor muscle (Bonasera and Nichols 1994; Nichols 1999). The points for the autogenic and compound responses were then fitted with second order polynomials (see Fig. 2). Confidence intervals (95%) were also computed for polynomials corresponding to autogenic responses or for polynomials corresponding to both autogenic and compound responses. Heterogeneous effects were detected by significant differences between the polynomials corresponding to autogenic and compound responses.

In some cases, the confidence intervals for a pair of polynomials were overlapping or the data points for the compound responses fell within the confidence limits for the autogenic responses. In this sense, the two polynomials were considered statistically indistinguishable for the range over which they overlapped. Overlapping confidence
intervals were observed under two conditions. First, when the mean values were very similar, the overlapping confidence limits indicated that for that range that the results were statistically indistinguishable. Second, when the range of background forces was so narrow that the confidence intervals were very wide, even substantial differences in mean were not statistically distinguishable. In the latter cases, the data were not included in subsequent analysis. Mechanical artifacts caused by mechanical interactions between muscles were detected by apparent heterogenic effects that were observed 10 ms after the initiation of stretch (Bonasera and Nichols 1996). Data in which these artifacts exceeded 5% of the autogenic response were rejected.

For each complete run using protocols 2 and 3, a number was calculated to express the amount of inhibition or excitation found for that muscle combination. For protocol 3, the force responses for each trial were calculated and integrated from 10 to 300 ms post stretch. The resulting integrated value for the compound responses was normalized to the integrated value of the autogenic response and translated into a percentage. For protocol 2, the area under the compound fitted line was normalized to the area under the autogenic fitted line and expressed as a percentage increase or decrease. A positive percentage indicated excitation (compound force response larger than autogenic force response), whereas a negative number indicated inhibition. The lines were not extrapolated beyond the last data point and the area under the fitted lines was computed, taking only those points in which both of the fitted lines have valid interpolated values.

Three-dimensional surfaces were also computed for the results using protocol 2. Compound and autogenic responses were measured every 5 ms as described in the preceding text for the data using protocol 1. Second-order polynomials were again computed for the compound and autogenic responses at each time point plotted against the initial forces in the donor muscle. The polynomials corresponding to the autogenic responses were then subtracted from the polynomials corresponding to the compound responses. The polynomials corresponding to these differences were then plotted together to form surfaces (Figs. 1–3). For the comparison of heterogenic effects from different muscles, the differences were normalized to the autogenic responses and therefore represent a percentage change due to the heterogenic input. The polynomials corresponding to the normalized differences were plotted together for all time points in the form of three-dimensional surfaces with time and force as independent variables (Figs. 6, 7, and 9).

**FIG. 2.** Heterogenic excitation among the vastus muscles. A: dynamic responses are shown for interaction from VL to VM. The autogenic (○) and compound (□) dynamic responses to 2 mm stretches were fitted with quadratic polynomials and 95% confidence limits. Inset: 2 force traces of VM at matched starting levels. Solid line, autogenic response; dotted line, the compound force response to 2 mm length change. Major tick marks on inset are 5 N apart. B: same as A with interaction from VM to VL. C and D: time expanded views of overlapping force traces from insets of A and B, respectively. To better estimate latencies of heterogenic reflexes. E: same as A with dynamic response shown for interaction from vastus intermedius (VI) to VL, as indicated in inset. F: same as A but with static interaction shown for same preparation. These data indicate that the reflex response was dominated first by excitation and then inhibition. G: a surface, computed as shown in Fig. 1, showing the transition from excitation during the beginning of the stretch phase to inhibition toward the end of the hold phase and the force dependence of the inhibition. The vertical axis refers to absolute differences between the compound and autogenic responses.
Measurement of latency

The latency of the heterogenic feedback was estimated in the following manner. Pairs of single force records of the recipient muscle from the autogenic and the compound responses were matched with respect to their initial force levels. After removing the baseline from these traces, they were plotted superimposed together with the calculated difference between the two traces. The latter was used as an aid to identify the time at which the two force traces diverge. Force traces were plotted on a time-expanded scale, concentrating on the region between −10 and +60 ms relative to stretch onset (Fig. 2, C and D). For each run up to eight matches were automatically generated. The time at which the force traces diverged was recorded in a database from which averages and SDs were calculated. For cases in which the diverging point could not be satisfactorily estimated, the corresponding time point would not be included in the average. This procedure was taken for results from protocol 2 as well as from protocol 3, and these results were pooled together in the database.

RESULTS

Short-latency excitation among V muscles

The heterogenic reflex effects among the V muscles were mainly excitatory under both quiescent and active conditions. An example of the excitation between VL and VM is shown in Fig. 1A for the quiescent condition. Stretch of either muscle alone evoked an excitatory response in the other, isometric muscle. When both muscles were stretched, both responses were significantly enhanced. These excitatory effects were also observed under active conditions (Fig. 2, A and B) and were little affected by force or time. The excitation from VL to VM was greater than the reverse in some preparations, but this asymmetry was not consistently observed and did not reach statistical significance across preparations (Table 1). Excitation between VI and VM was also consistently found, and the strength was observed to be greater in the direction VI to VM (Table 1).

Excitation was also observed between VL and VI (Table 1), but in the case of the reflex from VI to VL, the net excitation resulted from a balance between early excitation and late inhibition (Fig. 2, E–G). The excitation was marginally significant for the dynamic time point (Fig. 2E), became larger after termination of the ramp, and then gave way to inhibition later during the hold phase (Fig. 2, F and G). Excitatory effects were found in seven preparations, and the late inhibition was observed in four of these cases. In the remaining three cases, inhibition was suggested by declining excitation during the hold phase, and in one case the reflex remained excitatory with no decline throughout the hold phase.

The latencies of the excitatory reflexes among the V muscles were sharply defined (Fig. 2, C and D) and ranged between 18.6 and 20.8 ms, in agreement with the short-latency reflexes observed for other muscles in the cat hindlimb (Bonasera and Nichols 1994; Nichols and Houk 1976; Nichols et al. 1999) and with the distribution of monosynaptic excitation for the quadriceps muscles (Eccles et al. 1957). It was not possible to estimate the latency of the late inhibition from VI to VL, but the fact that this inhibition did not suppress short-latency excitation at high forces (Fig. 2G) indicates that it was slower than other types of force-dependent inhibition (Nichols 1999).

Mixed excitation and inhibition between V and RF muscles

Heterogenic feedback from all V muscles included inhibitory and weak excitatory components. The inhibition was often present under quiescent conditions, often increased with initial force, and could overcome the short-latency excitation. The strength of the inhibition is illustrated in Fig. 3A, where the static response of RF is plotted against the initial force of the VI, the donor muscle. The inhibition was evident during the ramp but also increased substantially during the hold phase (Fig. 3B), suggesting a second component of inhibition. This later inhibition from VI was large enough to cancel the autogenic response of RF. The inhibition from VL and VM to RF was only marginally significant and weaker than that from VI and was in no case sufficient to cancel the autogenic response of RF (Fig. 4, A and B).

The reflexes from RF to V were similarly distributed. The strongest inhibition was found to extend from RF to VI. This inhibition increased with force and suppressed the short-latency excitation at higher forces (Fig. 3C). The inhibition from RF to VL and VM was weaker and not strong enough to suppress the autogenic reflexes of these muscles (Fig. 4, C and D). These inhibitory reflexes could also be observed in some cases under quiescent conditions.

Evidence was obtained that the inhibition was sensitive to strychnine as is the case for reciprocal inhibition (Nichols and Koffler-Smulevitz 1991) and force-dependence inhibition in other muscle groups (Bonasera and Nichols 1994; Nichols 1999). In one preparation, strychnine was injected intravenously in increments up to a total of 150 μg. The inhibition from RF to VL was reduced progressively with each additional dose (data not shown). The inhibition was reduced by ~80% after the final increment had been delivered.

Latencies of heterogenic excitation and inhibition

The statistical results of the analyses of latencies are summarized in Table 2. This table includes measurements for both excitation and inhibition for the activated as well as the quiescent runs. The table only contains the shortest latencies observed among the quadriceps muscles. We did not attempt to

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**TABLE 1.** Magnitudes of heterogenic reflexes among the vastus muscles in percentage change

<table>
<thead>
<tr>
<th>Recipient</th>
<th>VI</th>
<th>VL</th>
<th>VM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>—</td>
<td>9.3</td>
<td>10.3</td>
</tr>
<tr>
<td>Range</td>
<td>—</td>
<td>3.0–18.0</td>
<td>9.6–38.7</td>
</tr>
<tr>
<td>Preparations</td>
<td>—</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>VL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>17.9</td>
<td></td>
<td>27.6</td>
</tr>
<tr>
<td>Range</td>
<td>2.6–32.2</td>
<td></td>
<td>19.1–65.5</td>
</tr>
<tr>
<td>Preparations</td>
<td>4</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>VM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>27.1</td>
<td>25.1</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>23.2–46.6</td>
<td>9.1–84.6</td>
<td></td>
</tr>
<tr>
<td>Preparations</td>
<td>3</td>
<td>4</td>
<td>—</td>
</tr>
</tbody>
</table>

For each animal, a mean value for each interaction was generated. These means were pooled across the preparations and median and ranges are given in this table. VI, VL, and VM, ratusus intermedius, lateralis, and medialis, respectively.
estimate the longer latencies because the departures were much less distinct. The data in Fig. 3B suggest two phases of inhibition, but it was not possible to calculate the onset of the longer latency. Even though inhibition from VM to RF could be observed when comparing force traces at the end of the hold-phase, the excitation was usually stronger earlier in the response, making an estimate of the latency of inhibition difficult. Latencies were compared using a two-way ANOVA. The excitatory and inhibitory pathways from RF to VL, RF to VM and VI to RF have indistinguishable latencies ($P < 0.05$). Latencies for excitation and inhibition were different only for RF to VI and for VL to RF ($P < 0.05$).

**Heterogenic reflexes from Q to individual triceps surae muscles**

After the investigation of heterogenic reflexes within Q, we studied the reflexes between Q and triceps surae (TS). Among the TS muscles, the nonsagittal components of torque differ significantly (Lawrence and Nichols 1999a,b; Lawrence et al. 1993). In the case of the Q, the VL and VM muscles pull in different directions on the patella but exert little nonsagittal torque on the tibia due to the patellar mechanism (Abelew et al. 1996). We tested whether these mechanical complexities were represented in the strengths of heterogenic reflexes between individual Q and TS muscles. Figure 4, E and F, shows that both VL and VM exert force-dependent inhibition on LG. Similar analyses were performed for all muscle combinations. There were no significant asymmetries attributed to the identity of the recipient or of the donor muscle. Because torque direction did not appear to have a major influence on the pattern of inhibition, we performed the remainder of the experiments on muscle groups defined by articulation, namely the single-joint S and V, and the two-joint G and RF.

**Inhibitory reflexes from TS to Q muscles**

Stretch of either S or G resulted in inhibition of both V and RF (Fig. 5). Excitatory effects were minimal or absent for all time points. The inhibition did not occur in temporally distinct components but instead increased smoothly with time. To examine how heterogenic pathways from different donor muscles were integrated, combinations of donor muscles were stretched.

The responses of RF to the stretch of the triceps surae muscles were less than the sum of the inhibitory responses from S and G (Fig. 5, A–C). The averaged percentage inhibition for both donors was 38%, while the sum of the two effects from S and G was 44%. Figure 5, D–F, shows the heterogenic effects measured within one preparation from muscles of the TS muscles onto the V group. Stretch of S had an average inhibitory effect of 15% and of G, 26%. Stretch of both TS groups led to an approximately summed inhibition of 44% (Fig. 5C). This analysis was also performed at different time points with the same overall result (data not shown) and seems to hold true across the range of initial forces, indicating approximately linear summation of heterogenic feedback from S and G to V. In the accumulated data across preparations, nearly linear summation was observed for the V and Q muscles but not for RF alone. Given the large contribution of forces from V to the Q group, the approximately linear summation of inputs from the TS muscles to Q muscles was probably due largely to the contribution of the V muscles. Nonlinear summation would be expected on the basis of cable properties (Burke 1967; Rall et al. 1967), but the factors that would affect the degree of linearity for the interactions investigated here are unknown.

The inhibition from the TS to the V muscles did not depend on the background force (Fo) of the donor to the same extent as did the inhibition to RF. This result could indicate that the inhibition for this muscle combination was not force dependent and did not arise from Golgi tendon organs. An alternative explanation is that the inhibition was from Golgi tendon organs but that the threshold to V was lower than for the inhibition to RF. It has been noted (Nichols 1999) that when the threshold of force dependent inhibition from G to S is low, the inhibition achieves a maximum at low forces and therefore becomes independent of Fo. The data in Fig. 5 are consistent with this explanation because the inhibition of V in response to the stretch of G or the combined TS muscles is large at low forces.
TABLE 2.  
Latencies of heterogenic pathways for quadriceps muscles

<table>
<thead>
<tr>
<th>Recipient</th>
<th>RF</th>
<th>VI</th>
<th>VL</th>
<th>VM</th>
</tr>
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<tbody>
<tr>
<td>RF</td>
<td>—</td>
<td>18.3 ± 2.9 (4)</td>
<td>16.6 ± 3.8 (21)</td>
<td>19.0 ± 2.1 (11)</td>
</tr>
<tr>
<td>Inhibition</td>
<td>—</td>
<td>23.4 ± 4.6 (11)</td>
<td>23.5 ± 3.5 (18)</td>
<td>*</td>
</tr>
<tr>
<td>VI</td>
<td>24 ± 5.7 (10)</td>
<td>—</td>
<td>17.8 ± 2.8 (18)</td>
<td>19.4 ± 3.4 (21)</td>
</tr>
<tr>
<td>Excitation</td>
<td>19 ± 2.5 (7)</td>
<td></td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>VL</td>
<td>19.8 ± 4.8 (21)</td>
<td>20.8 ± 3.1 (14)</td>
<td>—</td>
<td>18.6 ± 3.3 (22)</td>
</tr>
<tr>
<td>Inhibition</td>
<td>20.1 ± 4.7 (16)</td>
<td>↑</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>VM</td>
<td>25 ± 2.8 (2)</td>
<td>19.1 ± 3.1 (15)</td>
<td>19.1 ± 3.2 (30)</td>
<td>—</td>
</tr>
<tr>
<td>Excitation</td>
<td>23.5 ± 3.5 (2)</td>
<td></td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Latencies were measured from the onset of stretch to the departure of the compound response from the autogenic response (see METHODS). Means ± SD are reported with the sample size in parentheses. * No instances were found in which the short-latency inhibition from VM to rectus femoris (RF) was strong enough compared to the short-latency excitation to evaluate the latency of the reported heterogenic inhibition. † Excitation was in all instances stronger than the inhibition, therefore the latency of inhibition could not be measured, but was consistently larger than the excitation reported for this muscle combination.

FIG. 4. Examples of inhibitory reflexes among the quadriceps and triceps surae muscles. All plots depict the static responses of recipient muscles plotted against the initial forces in the donor muscles. Points corresponding to autogenic reflexes (○) are fitted by quadratic polynomials with confidence limits. Points representing compound responses (○) are fitted by quadratic polynomials (---). A–D: reflexes between vastus and RF muscles. E and F: force-dependent reflexes between vastus and VM muscles. E and F: force-dependent reflexes between vastus and VM muscles.
In general, G contributed more inhibition to the Q muscles than S (Fig. 5).

**Heterogenic reflexes from Q to the TS muscles**

The heterogenic feedback from Q to S included excitation as well as inhibition. At low initial force, the excitation from V to S achieved substantial levels during the plateau (Fig. 6A). This excitation occurred in two distinct phases, the first of which appeared with a latency of ~20 ms (Fig. 6A). This excitation declined and was replaced by inhibition as force increased, although evidence of the excitatory component could still be discerned at high forces (Nichols 1999). In the case of RF to S (Fig. 6B), no excitation could be detected, in agreement with previous studies showing excitatory reflexes only between single joint extensors (Eccles and Lundberg 1958). Inhibition appeared within 20 ms and increased during the plateau phase of the ramps up to ~125 ms after stretch. When RF and V were stretched together (Fig. 6C), the excitatory and inhibitory components summed approximately linearly at low forces. At higher forces, the inhibitory components summed less than linearly.

The inhibition from Q to G was purely inhibitory (Fig. 6, D–F). The combined percentage inhibition across preparations showed that the inhibition from the combined Q muscles was no greater than the contributions of either RF or the V muscles. When the force responses were recorded from the combined TS muscles (Fig. 7), the heterogenic feedback was predominately inhibitory as expected. The excitatory component from V to S was evident as a more rapid recovery of force in Fig. 7, A and C.

The preceding analysis provided a description of the interactions between heterogenic inputs and the stretch reflex. These interactions could, in principle, include postsynaptic influences on motoneuron excitability as well as presynaptic effects of the heterogenic feedback on autogenic reflex gain and tonic sensory input. To determine whether the heterogenic input had an effect on the recipient motor neurons that was independent of autogenic reflexes, we stretched the donor muscles and measured the responses in the isometric recipient muscles (protocol 1). Similar patterns of excitation and inhibition were observed when S and G were constrained isometrically, thereby minimizing autogenic reflexes (Fig. 8). Com-
Combinations of excitation and inhibition were received by S from V, whereas the other heterogenic reflexes contained predominantly inhibitory components that increased with background force and declined with time (Fig. 8, B–D). The inhibition was not evident at low initial forces because the isometric muscle was generating little or no force. As background force increased, the inhibition was not limited by the background force itself, indicating that the apparent force dependence did not result from saturation to zero net force. Another feature of the isometric responses was that the magnitudes of the inhibition were smaller than in the case of trials using protocol 2. This difference was likely to be due in part to the greater level of motor-unit recruitment when the recipient muscle was stretched. The inhibition of a population of larger motor units would have resulted in a larger decrease in force than in the case of the isometric recipient muscle. However, a contribution from presynaptic inhibition could not be excluded. A major role for postsynaptic inhibition, however, was supported by the strychnine sensitivity of this inhibition (see preceding text).

During the second extension phase or E2 of the step cycle, the ankle and knee joints flex, and therefore all extensor muscles spanning these joints undergo stretch (Goslow et al. 1973). The hip joint does not yield, so all four Q muscles presumably undergo similar length changes. To investigate the influence these heterogenic reflexes associated with the TS and Q muscles could potentially exert during this yield phase, the heterogenic input to each muscle group was evaluated by using the remaining muscles as donors, which were stretched simultaneously (Fig. 9) according to protocol 2. The stretch amplitude of 2 mm used in this study was similar to the magnitude of active lengthening during E2 for forward walking (Goslow et al. 1973). Although the extent of inhibition in intact animals is not known, the net effects observed in this experiment illustrated the extent to which excitatory and inhibitory influences can potentially compete and the relative influence of heterogenic inputs from local and more distant muscles.

The responses of S to stretch of the other three muscle groups consisted of excitatory components from V and G and inhibitory components from G and Q (Fig. 9A). In contrast, G received only net inhibition (Figs. 9B and 6). The known excitatory feedback from S to G may have reduced the onset of inhibition at low force and contributed to the recovery of force.

**FIG. 6.** Heterogenic reflexes from the quadriceps to subgroups of the triceps surae muscles. These 3-dimensional plots show the percentage increase (excitation) or decrease (inhibition) of compound responses over autogenic responses at 5-ms intervals throughout the responses. The resulting surfaces show the dependence of heterogenic reflexes on force and time. The reflexes from the quadriceps muscle group and its components to the soleus muscle (S) are shown in A–C and to the gastrocnemius muscles (G) in D–F.
at longer times. The strong inhibition from the TS to the V muscles was re-
lected in the profound and long-lasting inhibi-
tion resulting from the stretch of all three donors (Fig. 9C). The
excitation from RF was evident at low forces and early in the
responses but rapidly gave way to the large inhibitory in-
fluences from the three donors. The heterogenic inputs to RF were
characterized by greater excitation and less inhibition than to
the V muscles (Fig. 9D). The substantial excitation most likely
arose from the combined excitation from V. The net inhibition
onto both V and RF remained larger during the hold phase than
onto S and G, indicating the potential strength of force feed-
back from TS to Q.

DISCUSSION

We found consistent patterns of rapid excitatory and inhib-
itory feedback among the Q and TS muscles in intercollicular
decerebrate animals. The distribution of these reflexes was
similar to the organization of rapid feedback within the TS
muscle group, with two interesting differences that may be
related to the greater disparity in function between members of
the quadriceps muscles compared with members of the TS
group.

Mechanisms of heterogenic excitation

The patterns of excitation that we observed are generally
consistent with the findings of Eccles and coworkers (1957) on
monosynaptic Ia connections in anesthetized animals and pro-
vide some additional details concerning these projections. In
the latter study, VL and VM were grouped together as the V
muscle. The V muscle was linked strongly to crureus muscle
(VI) and both V and crureus muscles were linked weakly to
RF. Our results confirm this weighting and add further detail
because the four muscles were individually examined. The
strongest excitatory feedback was found in the linkages among
the V muscles. Strong pathways linked VL to VM, although
the strongest excitation was in the direction VL to VM in some
preparations. Strong excitation was also found from VI to VM.
The weakest excitatory pathways within the V group were
found to converge onto VI. Weaker still were the excitatory
linkages between each V muscle and RF. These results indicate
that the V muscles form a strong synergistic group with non-
uniform synaptic weights. The only instance of heterogenic
excitation across joints was found between V and S. A mono-
synaptic pathway from the VI to S has been demonstrated
electrophysiologically (Eccles et al. 1957). The present results
indicate that this pathway is sufficiently strong as to be evident
in the reflex interactions among multiple muscles (Fig. 9).

Mechanisms of heterogenic inhibition

Rapid heterogenic inhibition was distributed in a manner
that was largely complementary to the distribution of excita-
tion. This inhibition was absent among the V muscles but
present in the interactions between each V muscle and RF and
between the Q and TS muscles. Only in the case of heterogenic
reflexes from V to S was inhibition found to parallel excitation.
The inhibitory reflexes among the Q muscles were organized in
a similar manner to the pattern previously observed for the TS
muscles (Nichols 1994, 1999), except that inhibition was bi-
directional between V and S. The lack of inhibition from VL
and VM to VI along with previous motor-unit studies (Dacko
et al. 1996), allows us to reject the hypothesis that the inhibi-
tion is organized according to motor-unit type.

The latencies of rapid excitation and inhibition were not
significantly different. They were all in the range of 16–25 ms,
which compares favorably with previous estimates (Bonasera
and Nichols 1994; Nichols and Houk 1976). As argued previ-
ously (Nichols 1999), these latencies are consistent with path-
ways from group I and group II receptors. The similarity in
distribution between the heterogenic excitation reported here
and the monosynaptic pathways among the Q muscles (Eccles
et al. 1957), suggests that the excitatory reflexes are dominated
by pathways from group Ia afferents.

The force dependence of most of the rapid inhibitory ref-
xeses observed here suggests that pathways from Golgi tendon
organs play a prominent role in these linkages, although some
contribution from group II pathways cannot be excluded. It is possible that longer-latency components were present as well. Inhibition tends to develop slowly under similar conditions (Nichols 1999), so resolution of later components is difficult. The inhibitory response from VI to RF (Fig. 4) appeared to comprise a short-latency and a stronger, longer-latency component, but it was not possible to identify this later component as a separate reflex. For the case of VI to VL, the inhibition was present in only some preparations and comprised only a longer-latency component. This late inhibition occurred with latency in the range of 80–100 ms and could have been mediated by afferents in the group III or IV range. This inhibition had the

FIG. 8. Heterogenic reflexes from subgroups of the quadriceps muscles to subgroups of the isometric triceps surae muscles. These plots show the dependence of isometric force in response to stretch of the donor muscles (protocol 1) on force and time. Responses of S are shown in A and B and responses of G are shown in C and D.

FIG. 9. Heterogenic reflexes from combinations of 3 muscle groups. These plots are similar to those shown in Figs. 6 and 7. They show the combined heterogenic reflexes from 3 of the 4 muscle subgroups onto the 4th to illustrate the predicted effects in the intact limb.
magnitude and time course of clasp-knife inhibition but was distributed more locally than clasp-knife inhibition in cases of spinal injury (Cleland and Rymer 1990; Nichols and Cope 2001). In the case of spinal injury, the magnitude of clasp-knife inhibition is greatest in certain extensor muscles (Nichols and Cope 2001), but it does project to most extensor muscles including the muscle of origin. In the present case, the long-latency inhibition was observed to arise only from VI and project to VL and RF but not to VM or itself. The present results suggest that if the long-latency inhibition from VI to RF and VL does indeed arise from group III and IV afferents, that the associated interneurons have more specific and localized distributions than those associated with the clasp-knife reflex.

As was the case for the TS muscles, the inhibitory actions observed among the Q muscles were prolonged (Hayward et al. 1988; Nichols 1999). The inhibition did not decline rapidly during continued application of the stimulus as has been observed in the case of electrical stimulation (Heckman et al. 1994; Lafleur et al. 1993; Zytnicki et al. 1990). Instead, the inhibition remained strong for the duration of the stretch (250 ms) and in some cases was strong enough to reduce the force response of the recipient muscle to zero (Fig. 4B).

The strychnine sensitivity of this inhibition indicates that it is largely postsynaptic and glycineric. Previous mechano- graphic studies have shown that many of the intermuscular pathways evaluated under similar conditions are also strychnine sensitive. These reflexes include reciprocal inhibition between the tibialis anterior and S muscles (Nichols and Koffer-Smulevitz 1991), force-dependent inhibition between the G and S muscles (Nichols 1999) and force-dependent inhibition between the G and flexor hallucis longus muscles (Bonasera and Nichols 1994). There is evidence that there are linkages mediated by presynaptic inhibition between Q and TS in the cat (Misiaszek and Pearson 1997) and among hip, knee, and ankle in the human (Brooke and McIlroy 1985). Our data from both isometric and stretched recipient muscles do not exclude a role for presynaptic inhibition, but the accumulated evidence including the response to strychnine supports the hypothesis that postsynaptic inhibition does constitute an important component of the inhibition.

Although the inhibitory reflexes are most likely to be mediated largely by postsynaptic mechanisms, the possibility that they arise from recurrent pathways rather than proprioceptive pathways must also be addressed. The distribution of recurrent inhibition is generally organized to link muscles involved in stereotyped movements and locomotion (Hamm et al. 1987; Turkin et al. 1998). However, the effects of recurrent inhibition on motoneuron firing appear to be rather subtle (Lindsay and Binder 1991) and not great enough to affect static gain (Maltinfort et al. 1998). It is therefore unlikely that recurrent inhibition could produce a substantial inhibitory response. Finally, in animals selectively deprived of effective proprioceptive feedback by the reinnervation of muscles, force-dependent inhibition is absent along with stretch reflexes from the reinnervated muscles (Cope et al. 1994). We conclude that the rapid, force-dependent components of inhibition observed within and between the TS and Q muscles in the decerebrate cat result from actions of Golgi tendon organs.

**Role of heterogenic feedback in postural regulation**

Available evidence indicates that short-latency feedback is distributed according to architectural features of the musculoskeletal system (Eccles et al. 1957; Nichols 1994). Short-latency excitation links muscles that cross the same joint and that pull in approximately the same direction. Our results and those of Eccles et al. (Eccles et al. 1957) indicate that the V muscles form a strong synergistic group and that these muscles are only weakly linked to RF. Although the V muscles pull in different directions on the patella, the patellar mechanism redirects the forces of all the Q muscles into a nearly pure line of pull on the patella (Abelew et al. 1996).

The nonsagittal forces on the patella do have important functions within the knee joint mechanism, however. Deviations in patellar tracking can result in damage to the articular surfaces. Because VL and VM are the two muscles exerting large components of nonsagittal forces on the patella, these muscles are potentially very important for the correct tracking of the patella. The greater mass and potential force production of VL compared VM (Sacks and Roy 1982) suggests that some mechanism other than similarity of mechanical properties might contribute to balancing the forces of these muscles on the patella. In some preparations, we found heterogenic excitation to be stronger in the direction VL to VM. This nonuniformity in heterogenic excitation complements the disparity in intrinsic properties and could result in equalizing the stiffnesses of the two muscles, resulting in balanced pull on the patella. The inhibitory pathway from VI to VL could further improve patellar tracking because VM does not appear to receive this inhibition. We therefore suggest that the V muscles function as a group to perform the task of knee extension and the associated heterogenic reflexes reinforce the stiffness of this muscle group. This interpretation is consistent with previous ideas and results concerning the reflex interactions of synergistic muscles (Eccles et al. 1957; Lloyd 1946) if the organizing principal is based on global action of the muscles on the joint rather than the individual lines of action of the muscles.

The weakness of the excitatory reflexes between each vastus muscle and RF observed here as well as in the electrophysiological studies of Eccles and coworkers (Eccles et al. 1957) provides insights into the functional significance of short-latency or monosynaptic excitatory reflexes. It might be concluded that the weakness of these pathways is associated with the dissimilar activation patterns of RF and the V muscles (Engberg and Lundberg 1969; Rasmussen et al. 1978). Similarly, it has been suggested that the pattern of monosynaptic Ia connections is correlated with muscular “synergies” in motor coordination (Caicoya et al. 1999; Eccles and Lundberg 1958).

Application of this argument to other muscle groups, however, leads to a different interpretation. The TS muscles are often considered to be close synergists, and they exchange nonuniform but strong excitation (Eccles et al. 1957). These muscles are activated during the stance phase at all speeds of locomotion (Rasmussen et al. 1978) but become somewhat functionally dissociated at higher forces and higher speeds of locomotion (Fowler et al. 1993; Wallmsley et al. 1978). These patterns are consistent with the strong Ia connectivity among the TS muscles. However, the activation patterns diverge during stimulation of the caudal cutaneous sural nerve (Hagbarth
A similar dissociation between Ia linkage and patterns of activation has been noted for the long toe flexors (Bonasera and Nichols 1994; Dum et al. 1982; O’Donovan et al. 1982). Patterns of muscular activity during either voluntary movement or responses to cutaneous stimuli are clearly not restricted by these pathways.

In view of these and other data, it has been suggested that short-latency excitation contributes to the coordination of muscles during responses to postural disturbances rather than to patterns of voluntary activation (Nichols 1994; Nichols et al. 1999). In the case of TS, monosynaptic inputs from all three muscles enhance the stiffness of LG and MG and therefore strengthen the coupling between ankle and knee. In the case of the Q, the coupling between knee and hip is not as strongly enhanced by reflex excitation of RF from the V muscles. During locomotion in the cat, the knee and ankle joints remain closely in phase throughout the step cycle, but the hip follows a somewhat different trajectory (Goslow et al. 1973) in support of this interpretation. For example, the hip does not yield with the knee and ankle during the E2 phase of locomotion. These differences in coordination during the loading response correspond to the differences in strength of excitatory feedback in the two muscle groups.

The observed distribution of inhibitory-force feedback indicates that the underlying pathways do not serve to modulate strength of contraction of anti-gravity muscles in a global and uniform manner. In addition, inhibitory-force feedback does not appear to interfere with the coactivation of antigravity muscles. Instead, the nonuniform pattern of these pathways suggests a role in governing interjoint coordination (Nichols et al. 2002). The force feedback between the TS and Q groups parallels mechanical linkages of biarticular muscles between ankle and knee joints. Dorsiflexion of the ankle causes a mechanically mediated flexion moment at the knee through the G muscles and a neurally mediated decrease in knee extensor moment due to inhibition of the Q muscles (Nichols et al. 1999). Both mechanical and neural effects tend to distribute the perturbation between these joints and equalize the impedances of the two joints. The previously described inhibition from the G to S muscles (Nichols 1994) promotes this coupling of ankle and knee by suppressing the responses of the uniaxial S muscle in favor of the biarticular G muscles. The bilateral inhibition between the RF and V muscle can be interpreted as reducing the coupling between hip and knee, which action is consistent with the more independent motions of these two joints during locomotion (Goslow et al. 1973).

Cross-joint excitatory feedback observed during these studies was also nonuniform in that it was essentially unidirectional from the V to the S muscles. This linkage does not parallel mechanical linkages between knee and ankle because forced flexion of the knee would lead to an enhancement of the extensor moment at the ankle rather than the reduction that would accompany unloading of the G muscles. This pathway would also tend to accentuate differences in impedances of the two joints rather than equalize them (Nichols 1994). This action would be potentially disruptive of coordination if the pathway were to extend from the S to V muscles, but excitation in this direction was either small or masked by inhibition in these studies (see preceding text). In the observed case of a proximal distal projection, the action would be to enhance the mechanical contributions of the lighter, more distal segments to the net response of the limb to gravitational loads in a manner that would depend on the extent of yielding of the knee. We suggest that the excitatory pathways that project distally among uniarticular muscles compensate for the large proximal to distal gradient in the masses of limb segments (Hoy and Zernicke 1985).

The more prolonged actions of inhibitory-force feedback over those of excitatory-length feedback have implications for the dynamics of postural responses. The issue of stability has recurred in the literature and is potentially most critical in the presence of feedback (Prochazka 1996; Rack 1981). The necessity for stretch reflexes to have low gain is often cited. A more contemporary idea is that the gain of stretch reflexes automatically decreases due to the history-dependent properties of muscles and muscle spindle receptors (Lin and Rymer 2000). A neglected idea (Granit 1950) states that the inhibitory effects of force feedback could help stabilize the limb in the face of potentially destabilizing stretch reflexes. The impedance of the whole limb would depend on the summed effects of length and force feedback (Houk 1979; Nichols and Houk 1976), but the different time courses of the two kinds of feedback would favor higher compliance and enhanced coupling between limb segments after an initially stiff response. These effects of force feedback would, in principle, become more important at higher forces.

State dependence

During locomotion, the pathways described here apparently become integrated with widespread excitation from oligosynaptic linkages from muscle spindle receptors and Golgi tendon organs (Pearson 1995). It has been claimed that inhibitory-force feedback is actually replaced by positive-force feedback (Prochazka 1996), but this exclusion has not been demonstrated for all muscle groups and behavioral conditions. During fictive locomotion, group I excitation evoked by stimulation of muscle nerves extends from TS muscles to other muscles within that group as well as to Q muscles (Angel et al. 1996; Guertin et al. 1995). Excitatory actions in the direction Q to TS, however, were often small or inhibitory (Guertin et al. 1995). In a study of locomotion in premammillary decerebrate cats (Whelan et al. 1995), electrical stimulation of nerves from VL and VI muscles evoked responses in the TS muscles of variable sign. Studies using intermuscular stimulation in standing, intact animals (Pratt 1995) showed variable inhibitory and excitatory feedback for muscles in the TS group. In view of the variability of these results and the variety of experimental conditions and preparations, the issue of exclusivity of these pathways remains unclear. Recent mechanographic data suggest that group I excitation during locomotion is predominantly autogenic, while heterogenic force feedback remains inhibitory (Ross 2003; Ross et al. 2002). In most of the quoted studies, mixed effects were noted. Indeed, the presence of competing pathways from skin and muscle proprioceptors during normal movement would seem to be the normal mode of operation (Duysens et al. 1992; Lundberg et al. 1987). In the intercollicular decerebrate cat, inhibitory-force feedback does not interfere with the coactivation of antigravity muscles but can serve to coordinate responses among them (Nichols et al. 2002). This coordinating system could co-exist with excitatory
pathways that globally modulate the level of force of the antagonity apparatus.

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